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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/552,786

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EXAMINER

LEE, JAE W

ART UNIT

PAPER NUMBER

1656

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/552,786	<b>Applicant(s)</b> DEPERTHES ET AL.	
	<b>Examiner</b> JAE W. LEE	<b>Art Unit</b> 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 29 September 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 6,9,10,17,28-34,36,38-43 and 46-62 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 6, 9, 10, 17, 28-34, 36, 38-43 and 46-62 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Application status***

In response to the previous Office action, a non-Final rejection (mailed on 06/12/2007), Applicants filed a response and amendment received on 09/29/2008. Said amendment canceled Claims 1-5, 7, 8, 11-16, 18-27, 35, 37, 44 and 45, amended Claims 9, 10, 28, 39-43 and 46, and added Claims 47-62. Thus, Claims 6, 9, 10, 17, 28-34, 36, 38-43 and 46-62 are at issue and present for examination.

Upon further consideration of the amendment to claims filed on 05/12/2008, the previous restriction requirement mailed on 12/14/2006 is hereby withdrawn. Additional review of the disclosure led the Examiner to issue the instant restriction requirement, which further restricts the subject matter of previous Invention I. The Examiner regrets any inconvenience this may cause.

### ***Election/Restrictions***

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I: Claims 6, 9, 10, 17, 28-34, 36, 38-43 and 46-62, drawn to a recombinant inhibitor, or an inhibitor fragment thereof, which inhibits kallikrein, comprising a serpin sequence, comprising a modified Reactive Serpin Loop.

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For Group I, further restriction is required as shown below from Groups [1] to [2]

(NOTE: This is NOT a species election).

[1] Election of a single serpin sequence from the group consisting of alpha-lantichymotrypsin (ACT), protein C inhibitor (PCI), alpha-lantiproteinase (AAT), human alpha-lantitrypsin-related protein precursor (ATR), alpha-2-plasmin inhibitor (AAP), human anti-thrombin-III precursor (ATIII), protease inhibitor 10 (PI10), human collagen-binding protein 2 precursor (CBP2), protease inhibitor 7 (PI7), protease inhibitor leuserpin 2 (HLS2), human plasma protease C 1 inhibitor (C 1 INH), monocyte/neutrophil elastase inhibitor (M/NEI), plasminogen activator inhibitor-3 (PAI3), protease inhibitor 4 (PI4), protease inhibitor 5 (PI5), protease inhibitor 12 (PI12), human plasminogen activator inhibitor-1 precursor endothelial (PAI-I), human plasminogen activator inhibitor-2 placental (PAI2), human pigment epithelium- derived factor precursor (PEDF), protease inhibitor 6 (PI6), protease inhibitor 8 (PI8), protease inhibitor 9 (PI9), human squamous cell carcinoma antigen 1 (SCCA-1), human squamous cell carcinoma antigen 2 (SCCA-2), T4-binding globulin (TBG), Megsin, and protease inhibitor 14 (PI14), as listed in claim 9 is required.

[2] Election of **a single amino acid sequence representing the P6-P'6 of a modified Reactive Serpin Loop** is required, and furthermore, Applicants are required to point out which SEQ ID NO(s) from the group consisting of:

[i] SEQ ID NOs: 2, 4, 8, 10 and 14, as listed in claim 10;

[ii] SEQ ID NOs: 16, 17, 18, 19, 20, 21, and 22, as listed in claims 41 and 62;

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[iii] SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 56, SEQ ID NO: 58, and SEQ ID NO: 67, representing a structurally different P3 - P'2 amino acid sequence, as listed in claim 51;

[iv] SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 35, SEQ ID NO: 42, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 57, SEQ ID NO: 62, SEQ ID NO: 63, and SEQ ID NO: 66, representing a structurally different P4 - P'1 amino acid sequence, as listed in claim 53;

[v] SEQ ID NO: 31, SEQ ID NO: 43, SEQ ID NO: 46, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 60, SEQ ID NO: 61, and SEQ ID NO: 68, representing a structurally different P2 - P'3 amino acid sequence, as listed in claim 55; and

[vi] SEQ ID NO: 34, SEQ ID NO: 38, SEQ ID NO: 48, SEQ ID NO: 54, and SEQ ID NO: 59, representing a structurally different P1-P'4 amino acid sequence, as listed in claim 57,

correspond to **the single elected amino acid sequence representing the P6-P'6 of a modified Reactive Serpin Loop**. It is noted that SEQ ID NOs that are subsequences of the single elected amino acid sequence representing the P6-P'6 of a modified Reactive Serpin Loop, i.e., those SEQ ID NOs having overlapping scope with the single elected amino acid sequence representing the P6-P'6 of a modified Reactive Serpin Loop, will be examined on the merits.

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The inventions listed as Groups [1]-[2] and Groups [i]-[vi] do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

According to PCT Rule 13.2, unity of invention exists only when there is a shared same or corresponding special technical feature among the claimed inventions. All of the proteins, modified RSL sequences, and pentapeptides listed in Groups [1]-[2] and Groups [i]-[vi] represent *structurally distinct molecules* having different properties (emphasis added), i.e., having different amino acid sequences, difference in antibody recognition, etc., and therefore, they do not share the same technical feature. Although one may argue that the special technical feature between these Groups is that they all comprise a modified reactive serpin sequence that inhibits kallikrein, it is noted by the Examiner that such technical feature was known in the prior art. Chagas et al. (Determinants of the unusual cleavage specificity of lysyl-bradykinin releasing Kallikreins, Biochem. J., 1995, 306, pp: 63-69) teach a recombinant inhibitor of kallikrein, i.e., Abz-F-R-(note this arginine is at P1 position based on where the scissile bond is)-S-F-R-Q-EDDnp, (see peptide R14 on page 65, Table 2, which is not

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hydrolysed by human tissue kallikrein), along with other modified reactive serpin loop sequences having increased binding affinity to and increased inhibition of kallikrein (compare  $K_m$  and  $K_{cat}$  values on Tables 1-3 on page 65), which anticipates a recombinant inhibitor protein, or an inhibiting fragment thereof, which inhibits a kallikrein, comprising a serpin sequence comprising a modified Reactive Serpin Loop having a substituted P1-P1' scissile bond-containing pentapeptide, wherein P1 is an arginine (R) or a lysine (K) which results in increased binding affinity for said kallikrein. Taken together, Groups [1]-[2] and Groups [i]-[vi] lack the same or corresponding special technical feature, and unity of invention between the groups does not exist.

Applicant is advised that the reply to this requirement to be complete and must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(l).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jae W. Lee whose telephone number is 571-272-9949. The examiner can normally be reached on Monday through Friday from 8:30-7:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JAE W LEE/  
Examiner, Art Unit 1656

/Rebecca E. Prouty/  
Primary Examiner,  
Art Unit 1652